II. REMARKS

Preliminary Remarks

Amendment of the specification

The new paragraph added by the response filed on March 13, 2006, is amended by deleting the phrase 'the contents of which are incorporated herein by reference in their entirety.'

Amendment of the claims

In order to expedite prosecution, claims 1, 3-6, 31-51, 53, 55, 58, 59, and 66 are canceled, and claims 52, 54, 56, 60, 63-65, and 67 are amended. Upon entry of the amendment, claims 52, 54, 56, 57, 60-65, and 67 will be pending in the application.

Claims 52, 60, 63-65, and 67 are amended to identify the immunoreactive compound as an antibody or antibody fragment, as described in the specification, for example, on page 6, lines 24-26.

Claim 52 is amended to specify that the SMB apparatus of the invention comprises a 'plurality' of modules in fluid conducting communication with said apparatus, as described in the specification, for example, on page 2, lines 19-21. Claim 52 is also amended to include a step (f) of introducing an elution wash buffer into the module from step (e) in an elution wash zone, as described in the specification, for example, on page 4, lines 6-9, and is amended to include a step (g) of introducing a solution comprising a regenerant into the module from step (f) in a regeneration zone, as described in the specification, for example, on page 4, lines 9-12. Claim 52 is further amended to specify that step (h) comprises introducing an equilibration buffer into the module in an equilibration zone, wherein the equilibration buffer creates an environment in the module that permits binding of the antibody or antibody fragment to the solid phase comprising the ligand, as described in the specification, for example, on page 24, lines 17-19, and page 28, line 29, to page 29, line 1.

Claim 54 is amended to specify that step (g) of claim 52 comprises introducing a regeneration buffer that comprises urea into the module, as described for example on page 26, lines 15-16, and in claim 55, which is canceled.

Claim 56 is also amended to specify that step (g) of claim 52 comprises introducing a clean in place (CIP) solution into the module, as described for example on page 26.

No new matter has been added by virtue of the amendments or new claims. Applicants reserve the right to pursue canceled subject matter in a later filed divisional application.

Patentability Remarks

Objection to the specification

The examiner objects to the new first paragraph added by the previous response under 35 U.S.C. § 132(a), because the phrase "the contents of which are incorporated herein by reference in their entirety" is considered to be new matter. An amendment is submitted herewith that deletes the phrase to which the examiner objects, and withdrawal of the objection under 35 U.S.C. § 132(a) is respectfully requested.

35 U.S.C. §102(b) or alternatively 35 U.S.C. §103(a)

Claims 1, 3-5, and 31-33 are rejected under 35 U.S.C. §102(b) as anticipated by or, in the alternative, under 35 U.S.C. §103(a) as being obvious in view of Gottschlich (1997). Applicants respectfully disagree with the examiner's rejection; however, in order to expedite examination of this application, claims 1, 3-5, and 31-33 are canceled, and none of the rejected claims are pending. Withdrawal of this ground of rejection is therefore respectfully requested.

Claims 1, 3-4, 36-44, 46, 48, 51-54, 56, 58, and 62-67 are rejected under 35 U.S.C. §102(b) as anticipated by or, in the alternative, under 35 U.S.C. §103(a) as being obvious in view of Fulton (2001). Applicants respectfully disagree with the examiner's rejection; however, in order to expedite examination of this application, claims 1, 3-4, 36-44, 46, 48, 51, 53, 58, and 66 are canceled, and only claims 52, 54, 56, 62-65 and 67 of the rejected claims are pending.

To anticipate a claim under 35 U.S.C. § 102(b), the reference must teach every element of the claim. "A claim is anticipated only if each and every element as set forth in the claim is found, either expressly or inherently described, in a single prior art reference." Verdegaal Bros. v. Union Oil Co. of California, 814 F.2d 628, 631, 2 USPQ2d 1051, 1053 (Fed. Cir. 1987). "The identical invention must be shown in as complete detail as is contained in the ... claim."

Richardson v. Suzuki Motor Co., 868 F.2d 1226, 1236, 9 USPQ2d 1913, 1920 (Fed. Cir. 1989)." *See* M.P.E.P. § 2131.

Fulton fails to teach every element of the pending claims as amended. Fulton is a set of slide images that relate to the production of transgenic cows that produce milk containing human serum albumin (hSA) and to a design for a process that uses SMB affinity chromatography system to purify the hSA from the milk of the transgenic cows. The rejected claims are directed to a method of separating an antibody or antibody fragment from at least one immaterial component in a fluid mixture using a SMB apparatus. Fulton does not describe, either expressly or inherently, the claimed method of separating an antibody or antibody fragment from an immaterial component in a fluid mixture using a SMB apparatus. Fulton therefore does not anticipate the claimed invention, and withdrawal of the rejection of claims 52, 54, 56, 62-65 and 67 under 35 U.S.C. §102(b) as anticipated by Fulton is respectfully requested.

To establish a *prima facie* case of obviousness, the examiner must show that the prior art references themselves or the knowledge generally available to one of ordinary skill in the art would (1) provide some suggestion or motivation to modify or combine reference teachings to obtain the claimed invention, (2) teach or suggest all of the claim limitations, and (3) provide a reasonable expectation that the claimed invention can be made or used successfully. The teaching or suggestion to make the claimed combination and the reasonable expectation of success must both be found in the prior art, not in applicant's disclosure. See In re Vaeck, 947 F.2d 488, 20 USPQ2d 1438 (Fed. Cir. 1991), also In re Dance, 160 F.3d 1339, 1343, 48 USPQ2d 1635, 1637 (Fed. Cir. 1998) citing In re Raynes, 7 F.3d 1037, 1039, 28 USPQ2d 1630, 1631 (Fed. Cir. 1993); In re Oetiker, 977 F.2d 1443, 1445, 24 USPQ2d 1443, 1445 (Fed. Cir. 1992), and M.P.E.P. § 2142. Fulton fails to render obvious the claims of the present invention. The examiner states that in view of the knowledge generally available at the time the invention was made, it would have been obvious for one of ordinary skill in the art to modify the process proposed by Fulton for purifying hSA by "optimizing the steps proposed by Fulton" to obtain the claimed method of using a SMB apparatus to purify an antibody or antibody fragment (*see* page 3 of the official action). However, the examiner has failed to provide a scientific basis or support for this assertion, or any guidance or motivation to optimize Fulton's steps. Neither Fulton nor the general knowledge available at the time the invention was made would have motivated one of ordinary skill in the art to modify the process proposed by Fulton to obtain the claimed

method, nor would they have provided one of ordinary skill in the art with a reasonable expectation that the claimed invention could be used successfully. Accordingly, neither Fulton nor the knowledge generally available at the time the invention was made taught or suggested the claimed method that uses an SMB apparatus to purify antibodies or antibody fragments. In view of the foregoing remarks, the applicants submit that the examiner has failed to establish a *prima facie* case of obviousness, and therefore respectfully request that the rejection of claims 52, 54, 56, 62-65 and 67 under 35 U.S.C. §103(a) in view of Fulton be withdrawn.

35 U.S.C. §103(a)

Claims 5, 31-33, 49, 50, 59, and 60 are rejected under 35 U.S.C. §103(a) as being obvious in view of Fulton (2001), and further in view of Gottschlich (1997). The examiner alleges that the claimed process differs from that of Fulton "in reciting separating an immunoglobulin with Protein A or Protein G," and that it would have been obvious to modify the SMB process proposed by Fulton to obtain the claimed method, in view of the disclosure by Gottschlich that "IgG is purified with Protein A as a support in a simulated moving bed." See page 3 of the official action. Applicants respectfully disagree with the examiner's position. However, in order to expedite examination of this application, claims 5, 31-33, 49, 50, and 59 are canceled, and only claim 60 of the rejected claims is pending. Claim 60 is directed to the method of claim 52, wherein the antibody or antibody fragment comprises a constant region of an immunoglobulin and the solid phase comprises Protein A or Protein G.

Gottschlich discloses an experimental process for purifying antibodies that uses a SMB apparatus comprising a solid phase comprising Protein A which consists of four zones, an adsorption zone, a wash ('purge 2') zone, a desorption zone, and an equilibration ('purge 1') zone. However, Gottschlich does not describe or suggest the claimed method that uses an SMB apparatus comprising a solid phase comprising Protein A to purify an antibody or antibody fragment, wherein the SMB apparatus consists of at least the following six zones: an association zone, at least one wash zone, an elution zone, and elution wash zone, a regeneration zone, and an equilibration zone.

The applicants respectfully submit that at the time the invention was made, one of ordinary skill in the art would not have been motivated to combine Gottschlich with Fulton to

modify the SMB process for purifying hSA proposed by Fulton to obtain the method for purifying an antibody or antibody fragment as presently claimed. As discussed above, Fulton proposes an affinity chromatography process for purifying hSA from milk of unknown and unpredictable operability. One of ordinary skill in the art simply would not have been motivated to modify Fulton's proposed but untested SMB affinity chromatography process of unknown and unpredictable operability to utilize a different affinity ligand (protein A) for purification of a different protein (an antibody), with a reasonable expectation of success. Even if one of ordinary skill in the art who wished to practice the method of Fulton had considered the Gottschlich reference, they would not have had any suggestion or guidance from either reference for modifying the process proposed by Fulton to obtain the method as presently claimed. As discussed above, to establish a *prima facie* case of obviousness, the examiner must show that the prior art references themselves or the knowledge generally available to one of ordinary skill in the art at the time the invention was made would provide the suggestion or motivation to modify or combine reference teachings to obtain the claimed invention. *See* In re Vaeck, 947 F.2d 488, 20 USPQ2d 1438 (Fed. Cir. 1991), and M.P.E.P. § 2142. In the present case, the examiner has failed to show that either Fulton or Gottschlich, taken separately or in combination, or the general knowledge of one of ordinary skill in the art, would have provided suggestion or motivation to one of ordinary skill in the art to combine Gottschlich with Fulton to modify the process proposed by Fulton to obtain the method for purifying an antibody or antibody fragment as presently claimed. Neither the cited references nor the general knowledge of one of ordinary skill in the art described or suggested the claimed method that uses an SMB apparatus comprising a solid phase comprising Protein A to purify an antibody or antibody fragment, wherein the SMB apparatus consists of at least the six zones specified in claim 52, nor did they provide one of ordinary skill in the art with a reasonable expectation that the claimed invention could be used successfully. In view of the foregoing remarks, the applicants submit that a *prima facie* case of obviousness has not been established, and respectfully request that the rejection of claim 60 under 35 U.S.C. §103(a) in view of Fulton and further in view of Gottschlich, be withdrawn.

Claims 6 and 61 are rejected under 35 U.S.C. §103(a) as being obvious in view of Gottschlich (1997) as applied to claims 1, 3-5, and 31-33 above, and further in view of Garrone (U.S. Patent No. 5,595,085). The examiner alleges that the claimed process differs from that of Gottschlich in its use of an acidic buffer as the eluent, and that it would have been obvious to modify the SMB process described by Gottschlich to use an acidic buffer as the eluent, in view of the disclosure by Garrone. See page 4 of the official action. Applicants respectfully disagrees with the examiner's position. However, in order to expedite examination of this application, claim 6 is canceled, and only claim 61 of the rejected claims is pending. Claim 61 depends on claim 60, and is directed to a method for purifying an antibody or antibody fragment that uses an SMB apparatus comprising the six zones specified in claim 52 and a solid phase comprising Protein A as specified in claim 60, wherein the eluent comprises an acidic buffer.

As discussed above, Gottschlich describes an experimental process for purifying antibodies that uses a SMB apparatus comprising a solid phase comprising Protein A which consists of an adsorption zone, a wash zone, a desorption zone, and an equilibration zone. However, Gottschlich neither describes nor suggests the claimed method for purifying an antibody or antibody fragment that uses an SMB apparatus comprising a solid phase comprising Protein A, wherein the SMB apparatus consists of an association zone, at least one wash zone, an elution zone, and elution wash zone, a regeneration zone, and an equilibration zone. The disclosure by Garrone of the use of an eluent comprising an acidic buffer does not remedy the deficiencies of Gottschlich. Neither Gottschlich nor Garrone, taken separately or in combination, would have motivated one of ordinary skill in the art at the time the invention was made to modify the process described by Gottschlich to obtain the claimed method. In view of the foregoing remarks, the applicants submit that a *prima facie* case of obviousness has not been established, and respectfully request that the rejection of claim 61 under 35 U.S.C. §103(a) in view of Gottschlich, and further in view of Garrone, be withdrawn.

Claims 6 and 61 are rejected under 35 U.S.C. §103(a) as being obvious in view of Fulton (2001) and Gottschlich (1997) as applied to claims 5, 31-33, 49, 50, 59, and 60 above, and further in view of Garrone (U.S. Patent No. 5,595,085). The examiner alleges that the claimed process differs from that of Fulton, in view of Gottschlich, in its use of an acidic buffer

as the eluent, and that it would have been obvious to modify the SMB process of Fulton, in view of Gottschlich, to use an acidic buffer as the eluent, in view of the disclosure by Garrone. See page 4 of the official action. Applicants respectfully disagree with the examiner's position. However, in order to expedite examination of this application, claim 6 is canceled, and only claim 61 of the rejected claims is pending. As discussed above, claim 61 depends on claim 60, and is directed to a method for purifying an antibody or antibody fragment that uses an SMB apparatus comprising the six zones specified in claim 52 and a solid phase comprising Protein A as specified in claim 60, wherein the eluent comprises an acidic buffer.

For the reasons discussed above with respect to the rejection of claims 5, 31-33, 49, 50, 59, and 60 under 35 U.S.C. §103(a) in view of Fulton and Gottschlich, neither Fulton nor Gottschlich, taken separately or in combination, would have motivated one of ordinary skill in the art at the time the invention was made to combine Gottschlich with Fulton to modify the process proposed by Fulton to obtain a method for purifying an antibody or antibody fragment that uses an SMB apparatus comprising the six zones specified in claim 52 and a solid phase comprising Protein A as specified in claim 60, on which claim 61 depends, nor would they have provided one of ordinary skill in the art with a reasonable expectation that such a method could be used successfully. Accordingly, neither Fulton nor Gottschlich, taken separately or in combination, described or suggested the method of claim 60 for purifying an antibody or antibody fragment that uses an SMB apparatus comprising the six zones specified in claim 52 and a solid phase comprising Protein A. The disclosure by Garrone of the use of an eluent comprising an acidic buffer does not remedy the deficiencies in the teachings of Fulton in combination with Gottschlich. Fulton in combination with Gottschlich, and further in view of Garrone, therefore failed to provide motivation to one of ordinary skill in the art at the time the invention was made to combine the teachings of the cited references to obtain the method of claim 61, wherein the eluent comprises an acidic buffer. Accordingly, the cited references failed to describe or suggest all of the features of the claimed method. In view of the foregoing, the applicants submit that a *prima facie* case of obviousness has not been established, and respectfully request that the rejection of claim 61 under 35 U.S.C. §103(a) in view of Fulton and Gottschlich, and further in view of Garrone, be withdrawn.

Claims 34-35 are rejected under 35 U.S.C. §103(a) as being obvious in view of either Gottschlich (1997) or Fulton (2001), in view of Jiang (U.S. Patent No. 6,479,300) and Travis (U.S. Patent No. 4,016,149). Applicants respectfully disagree with the examiner's position. However, in order to expedite examination of this application, claims 34-35 are canceled, and none of the rejected claims is pending. Withdrawal of this ground of rejection is therefore respectfully requested.

Claims 36-44, 46, 48-54, 56, 58-60, and 62-67 are rejected under 35 U.S.C. §103(a) as being obvious in view of Gottschlich (1997), in view of Fulton (2001). The examiner alleges that the claimed process differs from that of Gottschlich in that the rejected claims are directed to a method that includes multiple wash zones and a CIP zone for cleaning in place, and that it would have been obvious to modify the SMB process described by Gottschlich to include multiple wash zones and a CIP zone. Applicants respectfully disagree with the examiner's position. However, in order to expedite examination of this application, claims 36-44, 46, 48-51, 58, 59, and 66 are canceled, and only claims 52, 54, 56, 60, 62-65, and 67 of the rejected claims are pending.

As discussed above, Gottschlich describes an experimental process for purifying antibodies that uses a SMB apparatus which consists of an adsorption zone, a wash zone, a desorption zone, and an equilibration zone. However, Gottschlich neither describes nor suggests the claimed method that uses an SMB apparatus comprising a solid phase comprising Protein A to purify an antibody or antibody fragment, wherein the SMB apparatus consists of an association zone, at least one wash zone, an elution zone, and elution wash zone, a regeneration zone, and an equilibration zone. The applicant respectfully submits that at the time the invention was made, one of ordinary skill in the art would not have been motivated to combine the teachings of Gottschlich with Fulton, It would not have been obvious to one of ordinary skill in the art to modify the SMB process for purifying antibodies described by Gottschlich in view of the diagram on page 16 of the Fulton reference, to obtain the claimed method that uses an SMB apparatus to purify an antibody or antibody fragment, with a reasonable expectation that the resulting SMB process would operate successfully.

With respect to claims 52 and 54, neither Gottschlich nor Fulton describes or suggests a method that uses an SMB apparatus to purify an antibody or antibody fragment wherein the

SMB apparatus comprises a regeneration zone. With respect to claims 63 and 64, neither Gottschlich nor Fulton describes or suggests a method that uses an SMB apparatus to purify an antibody or antibody fragment wherein the SMB apparatus comprises at least two wash zones between the association and elution zones, comprising a first wash zone in which a high salt wash is introduced, and a second wash zone in which a high salt wash is introduced. The cited references did not describe or suggest the claimed method that uses an SMB apparatus to purify an antibody or antibody fragment, wherein the SMB apparatus consists of at least the six zones specified in claim 52. In view of the foregoing remarks, the applicants submit that a *prima facie* case of obviousness has not been established, and respectfully request that the rejection of claims 52, 54, 56, 60, 62-65, and 67 under 35 U.S.C. §103(a) in view of Gottschlich in combination with Fulton be withdrawn.

Claims 37, 47, and 57 are rejected under 35 U.S.C. §103(a) as being obvious in view of Gottschlich (1997) and Fulton (2001) as applied to claims 36-44, 46, 48-54, 56, 58-60, and 62-67 above, and further in view of each of Abbot (U.S. Patent No. 4,430,496) and Yoshizako (U.S. Patent No. 6,641,735). The examiner alleges that the claimed process differs from that of Gottschlich in view of Fulton, in that the rejected claims are directed to a method that specifies the "use of an acid," and that it would have been obvious to modify the SMB process of Gottschlich in view of Fulton to use phosphoric acid as a CIP solution, in view of either Abbot or Yoshizako. *See* page 6 of the official action. Applicants respectfully disagree with the examiner's position. However, in order to expedite examination of this application, claims 37 and 47 are canceled, and only claim 57 of the rejected claims is pending. Claim 57 depends on claim 56, and is directed to a method for purifying an antibody or antibody fragment that uses an SMB apparatus comprising the six zones specified in claim 52, wherein step (g) comprises introducing a CIP solution into the module as specified in claim 56, wherein the CIP solution comprises phosphoric acid.

As discussed above with respect to the rejection of claims 36-44, 46, 48-54, 56, 58-60, and 62-67 under 35 U.S.C. §103(a) in view of Gottschlich in combination with Fulton, Fulton proposes an affinity chromatography process for purifying hSA from milk of unknown and unpredictable operability, and Gottschlich discloses an experimental process for purifying antibodies that uses a SMB apparatus which consists of four zones. As discussed above, to establish a *prima facie* case of obviousness, the examiner must show that the prior art references

themselves or the knowledge generally available to one of ordinary skill in the art at the time the invention was made would provide the suggestion or motivation to modify or combine reference teachings to obtain the claimed invention. *See* In re Vaeck, 947 F.2d 488, 20 USPQ2d 1438 (Fed. Cir. 1991), and M.P.E.P. § 2142. In the present case, the examiner has failed to show that either Gottschlich or Fulton, taken separately or in combination, or the general knowledge of one of ordinary skill in the art, would have provided any suggestion or motivation to one of ordinary skill in the art to combine Fulton with Gottschlich to modify the SMB process of Gottschlich to obtain the method for purifying an antibody or antibody fragment that uses an SMB apparatus comprising the six zones specified in claim 52, nor would they have provided one of ordinary skill in the art with a reasonable expectation that the claimed invention could be used successfully. Moreover, even if one of ordinary skill in the art who wished to practice the method of Gottschlich had considered the Fulton reference, they would not have had any guidance or motivation to modify the process of Gottschlich in view of Fulton to obtain the method of the present claims. The examiner has failed to establish a *prima facie* case that it would have been obvious to one of ordinary skill in the art at the time the invention was made to combine Fulton with Gottschlich to modify the SMB process of Gottschlich to obtain the method for purifying an antibody or antibody fragment that uses an SMB apparatus comprising the six zones of the claimed invention, as specified in independent claim 52. Accordingly, neither Gottschlich nor Fulton, taken separately or in combination, described or suggested a method for purifying an antibody or antibody fragment that uses an SMB apparatus comprising the six zones specified in claim 52, wherein step (g) comprises introducing a CIP solution into a module as specified in claim 56, on which claim 57 depends. The disclosure by Abbot of the use of phosphoric acid to clean an ion exchange column, and the disclosure by Yoshizako of the use of phosphoric acid to clean and pack a solid phase comprising a dye (Cibacron Blue) affinity ligands, do not remedy the deficiencies in the teachings of Gottschlich in combination with Fulton. Since Gottschlich in combination with Fulton, and further in view of Abbot or Yoshizako, failed to provide motivation to one of ordinary skill in the art at the time the invention was made to combine the teachings of the cited references to obtain the claimed method with a reasonable expectation of success, and as they fail to describe or suggest all of the features of the claimed method, as discussed above, the applicants submit that a *prima facie* case of obviousness has not been established, and respectfully request that the rejection of claim 57

under 35 U.S.C. §103(a) in view of Gottschlich and Fulton, and further in view of Abbot or Yoshizako, be withdrawn.

Claims 37, 47, and 57 are rejected under 35 U.S.C. §103(a) as being obvious in view of Fulton (2001), in view of each of Abbot (U.S. Patent No. 4,430,496) and Yoshizako (U.S. Patent No. 6,641,735). The examiner alleges that the claimed process differs from that proposed by Fulton in that the rejected claims are directed to a method that specifies the "use of an acid," and that it would have been obvious to modify the SMB process of Fulton to use phosphoric acid as a CIP solution, in view of either Abbot or Yoshizako. *See* page 7 of the official action. Applicants respectfully disagree with the examiner's position. However, in order to expedite examination of this application, claims 37 and 47 are canceled, and only claim 57 of the rejected claims is pending. As discussed above, claim 57 depends on claim 56, and is directed to a method for purifying an antibody or antibody fragment that uses an SMB apparatus comprising the six zones specified in claim 52, wherein step (g) comprises introducing a CIP solution into the module as specified in claim 56, and wherein the CIP solution comprises phosphoric acid.

For the reasons discussed above, *e.g.*, with respect to the rejection of claims 1, 3-4, 36-44, 46, 48, 51-54, 56, 58, and 62-67 under 35 U.S.C. §103(a) as allegedly being obvious in view of Fulton, neither the Fulton reference nor the general knowledge of one of ordinary skill in the art at the time the invention was made described, suggested, or provided motivation to one of ordinary skill in the art to modify the process proposed by Fulton to obtain a method for purifying antibodies or antibody fragments using a SMB apparatus comprising the six zones specified in claim 52, with a reasonable expectation of success. The teachings of Abbot and Yoshizako regarding the use of phosphoric acid as a cleaning agent in column chromatography do not remedy the deficiencies in Fulton and the general knowledge available at the time the invention was made. Therefore, it would not have been obvious to one of ordinary skill in the art to modify the process for purifying hSA proposed by Fulton, in view of either Abbot or Yoshizako, to obtain the method for purifying antibodies or antibody fragments using a SMB apparatus comprising a CIP zone wherein phosphoric acid is used as a CIP solution, as specified in claim 57.

Moreover, in view of the unknown and unpredictable operability of the method for purifying hSA proposed by Fulton, the significant differences between hSA and antibody proteins, and the recognized unpredictability of the art of protein purification, one of ordinary skill in the art could not have predicted if the method proposed by Fulton could be modified in view of either Abbot or Yoshizako to provide a method for purifying antibodies or antibody fragments using a SMB apparatus comprising a CIP zone according to claim 57, with a reasonable expectation that the resulting method would operate successfully. Accordingly, Fulton in combination with either Abbot or Yoshizako fail to describe or suggest the claimed method that uses an SMB apparatus to purify an antibody or antibody fragment, wherein the SMB apparatus comprises a CIP zone wherein the CIP solution comprises phosphoric acid as specified in claim 57. In view of the foregoing remarks, the applicants submit that a *prima facie* case of obviousness has not been established, and respectfully request that the rejection of claim 57 under 35 U.S.C. §103(a) in view of Fulton, and further in view of either Abbot or Yoshizako, be withdrawn.

Claims 45 and 55 are rejected under 35 U.S.C. §103(a) as being obvious in view of Fulton (2001), in view of Jiang (U.S. Patent No. 6,479,300) and Travis (U.S. Patent No. 4,016,149). The examiner alleges that the claimed process differs from that of Fulton in that the rejected claims are directed to a method that specifies the "use of a urea regeneration buffer," and that it would have been obvious to modify the SMB process of Fulton to use a urea regeneration buffer, in view of Jiang and Travis. *See* page 8 of the official action. Applicants respectfully disagree with the examiner's position. However, in order to expedite examination of this application, claims 45 and 55 are canceled, and none of the rejected claims is pending. As the subject matter of canceled claim 55 is incorporated into amended claim 54, this ground of rejection is considered to apply to claim 54. Claim 54 depends on claim 52, and is directed to a method for purifying an antibody or antibody fragment that uses an SMB apparatus comprising the six zones specified in claim 52, wherein step (g) comprises introducing a regeneration buffer comprising urea into the module.

For the reasons discussed above, *e.g.*, with respect to the rejection of claims 1, 3-4, 36-44, 46, 48, 51-54, 56, 58, and 62-67 under 35 U.S.C. §103(a) as allegedly being obvious in view of Fulton, neither the Fulton reference nor the general knowledge of one of ordinary skill in the art at the time the invention was made described, suggested, or provided motivation to one of

ordinary skill in the art to modify the process proposed by Fulton to obtain a method for purifying antibodies or antibody fragments using a SMB apparatus comprising the six zones specified in claim 52, with a reasonable expectation of success. The teachings of Jiang and Travis regarding the use of urea in column chromatography do not remedy the deficiencies in Fulton and the general knowledge available at the time the invention was made. Therefore, it would not have been obvious to one of ordinary skill in the art to modify the process for purifying hSA proposed by Fulton, in view of Jiang and Travis, to obtain the method for purifying antibodies or antibody fragments using a SMB apparatus that comprises a step of introducing a regeneration buffer comprising urea into a module, as specified in claim 54. Moreover, in view of the unknown and unpredictable operability of the method for purifying hSA proposed by Fulton, the significant differences between hSA and antibody proteins, and the recognized unpredictability of the art of protein purification, one of ordinary skill in the art could not have predicted if the method proposed by Fulton could be modified in view of Jiang and Travis to provide a method for purifying antibodies or antibody fragments using a SMB apparatus that comprises introducing a regeneration buffer comprising urea into a module according to claim 54, with a reasonable expectation that the resulting method would operate successfully. Accordingly, Fulton in combination with Jiang and Travis fail to describe or suggest the claimed method that uses an SMB apparatus to purify an antibody or antibody fragment, wherein the process comprises a step of introducing a regeneration buffer comprising urea into a module according to claim 54. In view of the foregoing remarks, the applicants submit that a *prima facie* case of obviousness has not been established, and respectfully request that the rejection of claim 54 under 35 U.S.C. §103(a) in view of Fulton, and further in view of Jiang and Travis, be withdrawn.

Claims 45 and 55 are rejected under 35 U.S.C. §103(a) as being obvious in view of Gottschlich (1997) and Fulton (2001) as applied to claims 36-44, 46, 48-54, 56, 58-60, and 62-67 above, and further in view of Jiang (U.S. Patent No. 6,479,300) and Travis (U.S. Patent No. 4,016,149). The examiner alleges that the claimed process differs from that of Gottschlich in view of Fulton in that the rejected claims are directed to a method that specifies the "use of a urea regeneration buffer," and that it would have been obvious to modify the SMB process of Gottschlich in view of Fulton to use a urea regeneration buffer, in view of Jiang and Travis. *See* pages 8-9 of the official action. Applicants respectfully disagree with the

examiner's position. However, in order to expedite examination of this application, claims 45 and 55 are canceled, and none of the rejected claims is pending. As the subject matter of canceled claim 55 is incorporated into amended claim 54, this ground of rejection is considered to apply to claim 54. As discussed above, claim 54 depends on claim 52, and is directed to a method for purifying an antibody or antibody fragment that uses an SMB apparatus comprising the six zones specified in claim 52, wherein step (g) comprises introducing a regeneration buffer comprising urea into a module.

For the reasons discussed above with respect to the rejection of claims 36-44, 46, 48-54, 56, 58-60, and 62-67 under 35 U.S.C. §103(a) in view of Gottschlich in combination with Fulton, neither Gottschlich nor Fulton, considered separately or in combination, would have motivated one of ordinary skill in the art at the time the invention was made to modify the process of Gottschlich to obtain the method for purifying an antibody or antibody fragment that uses an SMB apparatus comprising the six zones specified in claim 52, nor would they have provided one of ordinary skill in the art with a reasonable expectation that the claimed invention could be used successfully. The disclosure by Jiang of using urea in a buffer for "problem free operations," and the disclosure by Travis of using urea in a buffer as a regenerating agent do not remedy the deficiencies in the teachings of Gottschlich in combination with Fulton, and would not have motivated one of ordinary skill in the art at the time the invention was made to modify the process of Gottschlich to obtain a method for purifying an antibody or antibody fragment that uses an SMB apparatus comprising the six zones specified in claim 52, which process comprises introducing a regeneration buffer comprising urea into a module as specified in claim 54. Moreover, in view of the unknown and unpredictable operability of the method for purifying hSA proposed by Fulton, the significant differences between hSA and antibody proteins, and the recognized unpredictability of the art of protein purification, one of ordinary skill in the art could not have predicted if the method proposed by Fulton could be modified in view of Jiang and Travis to provide a method for purifying antibodies or antibody fragments using a SMB apparatus that comprises introducing a regeneration buffer comprising urea into a module according to claim 54, with a reasonable expectation that the resulting method would operate successfully. Since Gottschlich in combination with Fulton, and further in view of Jiang and Travis, failed to provide motivation to one of ordinary skill in the art at the time the invention was made to combine the teachings of the cited references to obtain the claimed method, and as

they failed to describe or suggest all of the features of the claimed method, as discussed above, a *prima facie* case of obviousness has not been established, and the applicants respectfully request that the rejection of claim 54 under 35 U.S.C. §103(a) in view of Gottschlich and Fulton, and further in view of Jiang and Travis, be withdrawn.

Claims 37, 47, and 57 are rejected under 35 U.S.C. §103(a) as being obvious in view Gottschlich (1997) and Fulton (2001) as applied to claims 36-44, 46, 48-54, 56, 58-60, and 62-67 above, and further in view of each of Abbot (U.S. Patent No. 4,430,496) and Yoshizako (U.S. Patent No. 6,641,735). This ground of rejection, which is stated on page 9 of the official action, is identical to the ground of rejection stated on page 6 of the official action. The applicant's response to this ground of rejection is stated above.

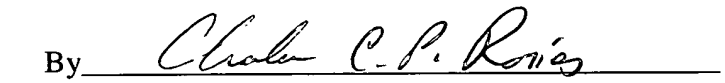
IV. IN CONCLUSION

All rejections having been addressed, it is respectfully submitted that the present application is in condition for allowance and a Notice to that effect is earnestly solicited. If the examiner identifies any points that he feels may be best resolved through a personal or telephone interview, he is kindly requested to contact the undersigned attorney at the telephone number listed below.

Please charge any fees or credit any overpayments associated with the submission of this response to Deposit Account Number 03-3975.

Respectfully submitted,

Date: October 2, 2006

By 

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